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ANDREA Q. RYAN			EXAMINER	
SANOFI-AVENTIS U.S. LLC			ANDERSON, REBECCA L	
1041 ROUTE 202-206				
MAIL CODE: D303A			ART UNIT	PAPER NUMBER
BRIDGEWATER, NJ 08807			1626	
			NOTIFICATION DATE	DELIVERY MODE
			04/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/749,631

Applicant(s)

KLEEMANN ET AL.

Examiner

REBECCA L. ANDERSON

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 is/are pending in the application.
- 4a) Of the above claim(s) 7-19, 21-32 and 34-48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5, 6, 20 and 33 is/are rejected.
- 7) ☒ Claim(s) 1-6, 20 and 33 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-48 are currently pending in the instant application. Claims 1, 2, 5, 6, 20 and 33 are rejected. Claims 1-6, 20 and 33 are objected. Claims 7-19, 21-32 and 34-48 are withdrawn from consideration as being for non-elected subject matter.

Election/Restrictions

Applicants' elected species of 3-guanidinecarbonyl-1-(7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-indole appears allowable over the prior art of record. Therefore, according to MPEP 803.02: should no prior art be found that anticipated or renders obvious the elected species, the search of the Markush-type claim will be extended. The search of the Markush-type claim was extended to include the products of the formula I wherein:

R1, R2, R3,n, Ra, Rb and **R4** are as found in claim 1 and **Ar** is 7H-pyrrolo-[2,3-d]-pyrimidine, which may be linked via any of its positions and which is substituted in at least one of its positions by alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, nitro, NRaRb, alkylcarbonylamino having 1,2,3 or 4 carbon atoms, hydroxyl, alkoxy having 1,2,3,4,5 or 6 carbon atoms, S(O)nR4, Co2H, alkoxycarbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylcarbonyl having 1,2,3,4,5 or 6 carbon atoms, CONRaRb, CN, polyfluoroalkyl having 1,2,3 or 4 carbon atoms, polyfluoroalkoxy having 1,2 or 3 carbon atoms or SO3H, or a racemic mixture, enantiomer, diastereomer, or tautomer of such compound, or a mixture thereof, or a pharmaceutically acceptable salt of such compound, racemic mixture, enantiomer, diastereomer, tautomer, or mixture.

Additionally, the search of the Markush-type claims was extended to the non-elected species of formula (I) wherein Ar is quinoline.

Prior art was found which anticipates the above identified nonelected species wherein Ar is quinoline. Since art was found on the nonelected species, subject matter not embraced by the elected embodiment or the above identified nonelected species is therefore withdrawn from further consideration.

It has been determined that the entire scope claimed is not patentable.

Response to Arguments

Applicant's arguments filed 16 January 2008 have been fully considered but they are not persuasive. In regards to the restriction requirement, Applicants traverse the restriction requirement as Lang does not disclose the N-bicycloheteroaryl substituents of the presently claimed indole derivatives, i.e. N-bicycloheteroaryl which may be linked via any of its positions and which is substituted in at least one of its positions by alkyl, halogen, nitro, NRaRb, alkylcarbonylamino, hydroxyl, alkoxy, S(O)nR4, CO2H, alkoxy carbonyl, alkylcarbonyl, CONRaRb, CN, polyfluoroalkyl, polyfluoroalkoxy or SO3H.

Applicants argue that Lang clearly discloses that when Y is NR(7), R(7) is R(8)-(CnH2n)-, and n is 0, then R(8) could be unsubstituted or substituted (C2-6)alkenyl, C3-10 cycloalkyl, phenyl, and unsubstituted quinolinyl or isoquinolinyl but not substituted quinolinyl or isoquinolinyl. This argument is not persuasive as column 4, lines 20-30 disclose that quinolinyl and isoquinolinyl can be unsubstituted or substituted by 1 to 3 substituents chosen from the group consisting of F, Cl, Br, I, etc.

Applicants argue that when Lang discloses that quinolinyl and isoquinolinyl can be substituted, it is only when R(1) to R(5) are R(8)-(CnH2n)-Z-, n is 0 and Z is a linker. This argument is not persuasive as claim 5 of Lang, which is dependent upon claim 1, claims R(8) as quinolyl or isoquinolyl which can be unsubstituted or substituted with substituents such as F, Cl, Br, I, CF3, etc. Therefore, claim 1 which states that R(8) can be quinolyl or isoquinolyl is including both unsubstituted and substituted quinolyl or isoquinolyl as dependent claim 5 further limits the variables for R(8) to be unsubstituted quinolyl or isoquinolyl or substituted by specific substituents such as F, Cl, Br, I, CF3, etc.

Applicants' additionally argue that in any of Lang's preferred embodiments wherein R(8) could be unsubstituted or substituted quinolinyl or isoquinolinyl, R(7) could not be an unsubstituted or substituted quinolinyl or isoquinolinyl. This argument is not persuasive as all of the preferred embodiments include R(7) as R(8)-CnH2n wherein n can be zero, therefore, R(7) can be unsubstituted or substituted quinolinyl or isoquinolinyl.

Therefore, Applicants' submit that Lang teaches against the nitrogen of the indole in the instant application being substituted by a substituted N-bicycloheteroaryl and Lang can not render obvious Applicants' claimed invention and the restriction should be withdrawn. As Lang discloses on column 4, lines 20-30 that quinolyl and isoquinolyl can be unsubstituted or substituted by 1 to 3 substituents chosen from the group consisting of F, Cl, Br, I, etc and since Lang discloses that quinolyl or isoquinolyl includes both unsubstituted and substituted, see claim 1 and dependent claim 5 for example, Lang is

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considered to teach that nitrogen of the indole can be substituted by a substituted N-bicycloheteroaryl and is considered to render the instantly rejected claims obvious.

Therefore, the restriction is considered proper.

Applicants' traverse the objection to the claims for the same reasons as found in the arguments to the restriction requirement. As the Lang reference is considered to render Applicants' instant claims obvious, the objection is maintained.

Applicants' traverse the 35 USC 103(a) rejection for the same reasons as noted in the restriction requirement arguments. As the Lang reference is considered to render Applicants' instant claims obvious, the rejection is maintained.

Maintained Claim Objections

Claims 1-6, 20 and 33 are objected to as containing non-elected subject matter. Claims 1-6, 20 and 33 presented drawn solely to the elected invention as identified supra would overcome the instant objection.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Claims 1, 2, 5, 6, 20 and 33 is rejected under 35 U.S.C. 103(a) as being obvious over LANG et al., US Patent No. 5,852,046.

Determining the scope and contents of the prior art

US Patent No. 5,852,046 discloses benzo-fused heterocyclic compounds having a 5-membered ring and their use as diagnostic agents and medicaments on column 1, lines 15-17. The benzo-fused heterocyclic compounds having a 5-membered ring are of the formula I wherein X and be N or CR(6); Y can be oxygen, S or NR(7); A and B together are a bond or are both hydrogen; one of the substituents R(1) to R(6) is $-\text{CO}-\text{N}=\text{C}(\text{NH}_2)_2$; the other respective substituents R(1) to R(6) are such as H or (C1-6)alkyl; n is zero to 10; R(7) can be hydrogen or R(8)-CnH2n; and R(8) can be hydrogen, (C2-6)alkenyl, phenyl, 1- or 2-naphthyl, pyridyl, quinolyl or isoquinolyl (columns 1 and 2). Preferences towards the subject matter of applicants' instant invention are found in the preferences wherein Y is NR(7) (column 2, line 29); one of the substituents R(1) to R(6) is $\text{CO}-\text{N}=\text{C}(\text{NH}_2)_2$; A and B are a bond (column 2, line 30); n is zero to 4 (column 2, line 41); R8 can be quinolyl or isoquinolyl (column 2, line 63). Further preferences to compounds which are positional isomers of the subject matter of the claimed invention are found in preferred embodiments on column 3 wherein X is CR(6); Y is NR(7); A and B together can form a bond; R(1) is $-\text{CO}-\text{N}=\text{C}(\text{NH}_2)_2$; n can be zero; R(8) can be quinolyl or isoquinolyl; and R97) can be R(8)-CnH2n. Further preferences are found on columns 3 and 4 wherein R(8) can be quinolyl or isoquinolyl and can be substituted by 1 to 3 substituents chosen from the group consisting of F, Cl, Br, I, CF3, etc.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the subject matter of the claims at issue is that the prior art does not specifically disclose a specific compound of the instantly claimed formula (I). However, the prior art discloses the compounds of the formula (I), which generically overlap with applicants' instantly claimed products and generically overlaps with positional isomers of applicant's instantly claimed products. Furthermore, the prior art does disclose preferences towards applicants' instantly claimed products and preferences towards positional isomers of applicants' instantly claimed products which provides direction and motivation to prepare the subject matter of applicants' instantly claimed invention.

Resolving the level of ordinary skill in the pertinent art

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the compounds within applicants instant compound of formula I when faced with the prior art of Lang et al. since the prior art discloses products, diagnostic agents and pharmaceutical compositions which generically overlap with the subject matter of the claimed invention and positional isomers thereof and provides direction towards applicants' subject matter of the instant claims within the preferred embodiments. The motivation would be to the expectation of preparing more biologically active benzo-fused heterocyclic compounds useful as diagnostic agents and as pharmaceutical compositions for the treatment of conditions such as atherosclerosis. Furthermore, nothing unobvious is seen in substituting the claimed isomer for the structurally similar isomer, as taught by LANG et al. since such structurally related

compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. In re Norris, 84 USPQ 458 (1950).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Rebecca Anderson/
Primary Examiner, AU 1626*

12 April 2008

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